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TITLE: <input type="checkbox"/> PROGRESS REPORT <input checked="" type="checkbox"/> PHASE REPORT <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> TERMINATION REPORT Effect of Feeding Various Combat Rations and Effect of Adverse Environment on Pancreatic Digestion			
SUMMARY			
<p>A BIBLIOGRAPHY OF RESEARCH ON THE EXTERNAL SECRETION OF THE PANCREAS.</p> <p>ARMY MEDICAL SEP 26 1950 LIBRARY</p>			

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## INTRODUCTION

The purpose of this bibliography is to present in concise form the experimental work on the effect of various stimuli, particularly food, on the quality and quantity of external pancreatic secretion and on pancreatic function tests. The period covered extends from 1890 to January, 1946.

A great deal of the material was obtained from Chemical Abstracts and Nutritional Abstracts and Reviews. The journals containing the greatest amount of material on the subject are American Journal of Physiology, American Journal of Digestive Diseases, Gastroenterology, and Pfluger's Archiv fur die Gesamte Physiologie.

Section I contains references which were concerned with the determination of 'normal' enzyme output. However, practically all the articles in sections II - IV will also be found to contain data on the normal enzyme output of the pancreas.

The numerous studies made on the effects of secretin, histamine and drugs acting through the nervous system on pancreatic secretion are not included in this report, except when other stimuli were used along with them.

For a rather complete picture of the experimental work done up until 1928, Die Aussere Sekretion Der Verdauungsdrusen by Rabkin is recommended. His later book, Secretory Mechanisms of the Digestive Glands, gives a comprehensive review of the work done since that time. Lagerlof's book, Pancreatic Function and Pancreatic Disease, gives a complete review of the

work done on function tests using duodenal content analysis,  
but many articles on the subject have appeared since it's  
publication (1942).



Experimental observations in the case of the pancreas  
of the dog

By J. J. Cannon, M.D., Harvard Medical School, Boston, Mass., U.S.A.

By normal means there are no cells which secrete  
any substance except the cells of the pancreas which  
secrete the pancreatic juice. In the case of the  
pancreas the secretion is maintained at an even level. The secretion  
and quality of the juice can be varied. The  
secretion can be varied.

### Experimental observations in the case of the pancreas

By J. J. Cannon, M.D., Harvard Medical School, Boston, Mass., U.S.A.

## SECTION I

### NORMAL PANCREATIC SECRETION

The normal secretion of the pancreas is a fluid which  
is secreted by the cells of the pancreas.

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is secreted by the cells of the pancreas.

Pancreatic Secretion in Man after Intravenous Administration of Secretin

G. Agren and H. Lagerlof. Acta. Med. Scand. 90, 1 (1936)

On normal subjects there are no ill effects after giving secretin repeatedly. After administration of secretin there is a washing out of stored enzymes but afterward the secretion is sustained at an even level. The concentration and quality of the enzymes run parallel. Normal values are given.

Continuous Pancreatic Secretion in the Rabbit

S. G. Baxter. Am. J. Physiol. 96, 341 (1931)

In the rabbit there is a true "spontaneous" secretion of pancreatic juice, which may be increased by exogenous stimuli, such as acid, bile and peptone, present in the duodenum and small intestine.

The External Secretion of the Pancreas

W. Berger, J. Hartmann and H. Loubner. Klin. Wochschr. 14, 490 (1935) CA. 30:8325<sup>5</sup>

The authors claim to be able to follow in the human subject the course of amylase and trypsin excretion by the pancreas, using a duodenal tube and fractional sampling at 2 to 5 minute intervals. Curves are given for these enzymes.



Functional Exploration of the Pancreas

M. Chambon, P. Mallet-Guy and J. Folliot. Compt. Rend. Soc. Biol. 127, 632 (1938) CA. 32:4186<sup>9</sup>

The determination of the lipolytic activity of human pancreatic juice is described. Normal values are given.

The Concentration of Pancreatic Enzymes in the Duodenum of Normal Persons and Persons with Disease of the Upper Part of the Abdomen

M. W. Comfort, R. L. Parker, A. E. Osterberg. Am. J. Dig. Dis. 6, 249 (1939)

Normal values for trypsin, lipase and amylase are given. A marked contraction of the range of concentrations of these was found in patients with carcinoma of head of pancreas, and of the ampulla of Vater, and chronic atrophic pancreatitis with steatorrhea.

The Lipolytic Analysis of Duodenal Contents

B. H. Craver and B. S. Walker. Am. J. Dig. Dis. 9, 223 (1942)

A simple clinical method of lipolytic analysis is described which is applicable to duodenal contents. The results of fifty intubations on normal subjects are reported to serve as a standard of reference.

The Clinical Application of Secretin in the Study of Pan-  
creatic Function

J. S. Diamond and S. A. Siegel. N.Y. State J. Med. 41, 869  
(1941)

The use of the secretin test on 90 patients, both normal and with pathological conditions is described, and the findings discussed. It was found that in pathologic states of the pancreas the enzyme production first became affected; the volume and bicarbonate were more stable and less easily disturbed.

Study of the Enzyme Activities of Duodenal Contents as a  
Means of Evaluating Pancreatic Function

A. H. Free, A. J. Beams and V. C. Myers. Gastroenterology 1,  
183 (1943)

Quantitative determinations of enzyme activity were carried out in a group of normal subjects during fasting and after stimulation of the pancreatic secretion with olive oil. On the basis of results obtained in these subjects a system of evaluating pancreatic secretory activity is described.

Fractional Analysis of the Duodenal Contents in Normal  
Individuals

J. Friedenwald and J. Sindler. J. A. M. A. 77, 1469 (1921)

The findings on ten normal individuals are given.



Human Pancreatic Secretion Studied from a Case of Pancreatic Cyst and Fistula

J. Kahn and H. M. Klein. Am. J. Med. Sci. 184, 503 (1932)

The pancreatic fluid was collected postoperatively by a drainage tube inserted into the cyst cavity. It continued flowing for 59 days after insertion of tube. No constancy was found in the ratio lipase: trypsin: amylase secreted. The daily output of these enzymes, when compared with their amounts estimated to be present in the gland, was found to represent a large proportion of the lipase present and a much smaller amount of the amylase and trypsin. The latter was found to be free of enterokinase.

New Methods for Estimating Enzymatic Activities of Duodenal Contents of Normal Man

C. W. McClure, A. S. Wetmore and L. Reynolds. Arch. Int. Med. 27, 706 (1921)

Methods of determining proteolytic, lipolytic and amylolytic enzymes are discussed, and their shortcomings in using them for analysis of the enzymes of duodenal contents are pointed out. The authors' methods for the determining of these enzymes in duodenal contents are given in detail, and their accuracy is discussed.

Studies in Old Age. IV. The Clinical Significance of Salivary, Gastric and Pancreatic Secretion in the Aged.

J. Moyer and H. Necheles. J. A. M. A. 115, 2050 (1940)

In old age there is a decrease in salivary, gastric and pancreatic secretion (except amylase), both in quantity and enzyme content. The diminution in quantity of secretion apparently does not affect intestinal digestion. Values for secretions obtained at different ages are given.

Physiologic Observations on Patients with External Pancreatic Fistula

J. M. Miller and T. B. Lipor. Ann. Surg. 120, 852 (1944)

Normal pancreatic secretion and the secretion with various nutritional and pharmacological stimuli are given for three patients with pancreatic fistulas.

Studies on Old Age. V. Active Pancreatic Secretion in the Aged.

H. Necheles, F. Plotke and J. Moyer. Am. J. Dig. Dis. 9, 157 (1942)

The pancreatic secretion of a group of 30 aged subjects with an average age of 66.5 years was compared with that of a group of 30 young persons with an average age of 23.4 years. Pancreatic secretion was stimulated by intraduodenal injection of oleic acid. Bicarbonate and amylase content was significantly increased in the older group; lipase was 21% lower. Volume of fluid and trypsin concentration were not significantly different in both groups.



An Analysis of the Duodenal Drainage in the Steathorrheas

H. F. Philipsborn, Jr. et.al. J. Pediatrics 26, 107 (1945)

The duodenal contents of normal children, "feeding problems", and children with pancreatic diseases were analyzed for enzymatic activity, and the values obtained are given. "Feeding problems" may be due to temporary pancreatic insufficiency.

Physiology of the Pancreatic Secretion of Man Studied by Means of a Fistula of the Duct of Wirsung

M. Villaret and L. Justin-Besancon. Nutrition (Paris) 6, 209 (1936)

The analysis of the pancreatic juice of a patient is given, both 'normal' and as a result of various stimuli. The findings of other workers as regards the volume of juice secreted by humans are listed.

Continuous Pancreatic Secretion

T. F. Zucker, F. G. Newburger and R. W. Berg. Am. J. Physiol. 102, 193 (1932)

In dog with cannulated pancreas the secretion is continuous, but food or the injection of secretin temporarily increases the rate of flow. Anaesthesia may completely inhibit the flow of pancreatic juice. Ether increases the amylase level of the blood.

## SECTION II

### EFFECTS OF FOODSTUFFS AND FOOD PRODUCTS ON SECRETION OF PANCREATIC JUICE

- a. Protein and Protein Derivatives
- b. Fats, Fatty Acids and Soaps
- c. Vitamins
- d. Mixed Diets and Comparative Studies



a. Protein and Protein Derivatives

The Secretory Stimulative Effect on the Pancreas of the  
Amino-Acid Hydrochlorides

M. Arai. Biochem. Z. 121, 175 (1921) CA. 15:3687<sup>4</sup>

Injection into the duodenum of dogs with pancreatic fistulas of aqueous solutions of the HCl salt of glycocoll, d-alanine, d-glutamic acid and glycylglycine stimulated pancreatic secretion. The HCl of histidine and d-glucosamine did not act as stimulants. Adrenaline depressed the stimulating action of these compounds.

The Influence of Sodium Nitrite, Peptone and Pilocarpine on  
the External Secretion of the Pancreas

O. W. Barlow. Am. J. Physiol. 81, 189 (1927) CA. 21:2507<sup>6</sup>

Peptone, histamine and  $\text{NaNO}_2$  given intravenously increased the external pancreatic secretory rate, presumably by improving nutritional conditions, i.e., blood supply to the splanchnic organs.

Action of Amino Acids on the Pancreatic Secretion

A. Frouin. Compt. Rend. Soc. Biol. 74, 131 (1913) CA. 7:1374<sup>3</sup>

Final products (glycocoll, leucine, alanine, tyrosine, asparagine, aspartic acid, glytamic acid) of the digestion of proteins had no effect on the secretory activity of the pancreas when introduced in various concentrations by intravenous injection. When introduced directly into the intestine they



did increase the secretion somewhat, but this is ascribed to the pH of the substances for it did not occur after neutralization. Peptone has no effect on the secretory activity when introduced into the intestine, but inhibits the action of mineral acids in exciting secretion.

Influence of Peptone on the Secretory Action of Mineral and Organic Acids on Pancreatic Secretion

A. Frouin and S. Marbe. Compt. Rend. Soc. Biol. 68, 176 (1910) CA. 4:2017<sup>5</sup>

The addition of peptone hinders the formation of secretin by mineral acids, although it increases the quantity of secretin set free by organic acids.

Influence of the Products of Digestion of Proteins and Sugars on the Secretory Power of Acids on the Intestine

A. Frouin and M. de Medeiros. Compt. Rend. Soc. Biol. 68, 174 (1910) CA. 4:2017<sup>6</sup>

In animals with pancreatic fistulae peptone decreased the secretory action of HCl, although it increased that of lactic acid. Lactose and saccharose increased the secretory action of organic acids. Lactose increased the action of HCl. Hence, among carnivora pancreatic and enteric secretions are not abundant because the albumoses and peptones formed by

stomach digestion diminish the secretory action of the gastric juice on pancreatic and intestinal secretion. With the herbivora fed on carbohydrates and organic acids the pancreatic and enteric secretions are more abundant. The secretory power of organic acids is increased by the products of digestion of proteins and by sugars. The quantity of intestinal and pancreatic secretions can be controlled by the ingestion of peptones, of sugars, or of organic acids.

Relationship between Mechanical State of the Feed (Meat) and Pancreatic Secretion

W. H. Gantt and P. S. Kupalow. Z. f. d. ges. Exp. Med. 56, 802 (1927)

Experiments were performed on 2 dogs with Pavlov pancreatic fistulae that were fed pieces of meat or ground meat. The volume and dry weight of the secretion were determined. It was found that the volume was greater and the percent dry weight was less when pieces of meat were fed. However, the total dry solids were 2 - 3 times greater when pieces of meat were fed than when ground meat was fed. It is concluded that the work of digestion is less when ground foods are fed.



Is a Portion of the Pancreatic Secretory Response to a Meal  
Due to the Absorption of Digested Food Products

J. Gray, M. S. Kim and A. C. Ivy. Am. J. Physiol. 116, 210  
(1936)

The pancreatic secretion of anaesthetized dogs with cannulated pancreatic ducts was measured after intravenous injections of various substances. Untreated liver extract containing some vaso-depressor substances caused a two-fold increase in the continuous secretion; liver extract freed of vaso-depressor activity was inert. Liver extract plus secretin didn't act synergistically. Witte peptone caused very slight increase of flow. Dextrose and emulsified fats caused no increase in flow. Concludes that secretin is probably the only humoral agent concerned in the secretory response of the pancreas to a meal.

The Action of the Nitrogenous Bases of the Gastric Juice on  
Blood Pressure, Pancreatic Secretion and Flow of Bile

S. A. Komarov. Am. J. Physiol. 115, 604 (1936)

Dogs with cannulated pancreatic and bile ducts were injected intravenously with the test solutions. The histidine fraction isolated from canine gastric juice produced no effect on blood pressure, pancreatic secretion or flow of bile. The arginine fraction exhibited a histamino-like action on

the blood pressure and the secretion of pancreatic juice. It had no definite effect on the secretion of bile. The lysine fraction possessed a marked pressure activity and stimulated the secretion of pancreatic juice and bile. None of these effects were influenced by preliminary section of the vagi or by atropinization.

The Effect of Certain Fractions of Meat Extract on the Secretion of Pancreatic Juice and Bile

R. Krimberg and S. A. Komarov. Biochem. Z. 184, 442 (1927)  
CA. 21:2309<sup>1</sup>

The largest part of the phosphotungstic acid ppt. of meat extract which stimulates secretion of pancreatic juice is in the carnosino-methylguanidine fraction. Authors state that carnosine isn't stimulant, but methylguanidine plays a role.

Restoration of the Pancreatic Secretion by Peptone and Histamine

M. E. McKay and S. G. Baxter. Am. J. Physiol. 98, 42 (1931)

In anaesthetized dogs and cats with cannulated pancreas the pancreatic response may be restored by injecting into the duodenum 0.2% HCl plus 10 - 30 gms. histamine when it has become exhausted by repeated injection of 0.2% HCl.



Witte's peptone may be substituted for histamine and get same result. The previous feeding of the animals is an important factor in these experiments.

(Usual commercial preparations of peptone contain considerable quantities of histamine (W. Feldberg and E. Schilf, Histamine, Berlin, (1930), pg. 40))

Effect of Albumin and Casein Cheese on the Activity of the Gastrointestinal Tract

M. I. Olevskii, L. Zelenko and S. Kuz'menko. Med. Exptl. (Ukraine) 12, 64 (1935) CA. 31:1476<sup>3</sup>

On dogs with chronic fistulas casein cheese produced somewhat smaller quantities of pancreatic juice than albumin cheese.

The Pancreatic Secretagogue Action of Products of Protein Digestion

J. E. Thomas and J. O. Crider. Am. J. Physiol. 134, 656 (1941)

Pancreatic juice was collected from dogs by means of a cannulated duodenal fistula. Effective drainage of stomach was maintained during experimental periods. Products of protein digestion acted in the intestine as stimuli for the external secretory function of the pancreas. Their effective-

ness is not dependent on the coincident flow of bile into the intestine nor on the secretagogue action of water or acid. The secretion produced by peptone stimulation has a higher specific gravity and contains many times more N/o.c. than that produced by water, acid, or secretin. Among commercial peptones the more effective are those having the higher percentage of proteose. The secretion could not be produced by secretin alone. The secretion elicited by peptones resembles that caused by pilocarpine and other stimuli acting through or on the secretory nerves. Conclusion is drawn that peptones act through a nervous mechanism.

Changes in the Acinar Cells of the Pancreas in Response to the Presence of Peptone in the Small Intestine

A. J. Ramsay, J. L. Thomas and J. O. Crider. Anat. Rec. 86, 87 (1943)

Peptone was introduced into the duodenum of unanesthetized dogs with partially exteriorized pancreas by means of an injection tube. During peptone stimulation the acinar cells become depleted of zymogen granules and secretion accumulates in the ducts. Acinar cells in the vicinity of the islets retain their granules, some forming halos. The changes are similar to those described as occurring during stimulation of the vagus and differ from those said to result from presence of Hcl in intestine. They did not occur in vagotomized animals.



Influence of Certain Foods and of Emotion on Pancreas  
Secretion

Togami. Z. Physik.-Diat. Ther. 12, 453 (1909) CA.3:2312<sup>9</sup>

When dogs with Pavlov pancreatic fistulas are fed with asparagus, spinach, carrots, or cauliflower, little stimulation of pancreatic juice was observed. Meat broth produced a marked stimulation. Anger or other psychic disturbances inhibit the flow.

Contributions to the Physiology and Pharmacology of the  
Pancreas

B. N. Vailiev. Arch. d. Sc. Biol. 2, 219 (1893)

(From The Work of the Digestive Glands, I. P. Pavlov, 1910)

P. 44 If a dog is fed for weeks on milk and bread, and then given an exclusively meat diet, containing more proteid but scarcely any carbohydrate, a continuous increase in the proteid ferment of the juice is observed. The ability to digest proteid increases from day to day, while the amylolytic power of the juice decreases.

b. Fats, Fatty Acids and Soaps



The Mechanism of the Action of Fat as a Secretory Excitant  
of the Pancreatic Glands

B. P. Babkin and H. Ishikawa. Arch. Ges. Physiol. 147,  
288 (1912) CA. 7:1223<sup>2</sup>

After subcutaneous injection of 0.005 g. atropine the usual slight secretion of pancreatic juice was not inhibited. When the injection occurs at the height of the pancreatic activity induced by fat in the intestine there is no effect produced on the volume of the secretion but its content of solid matter and ferments is greatly reduced. If the atropine is first injected, the introduction of neutral fat or oleic acid fails to induce increased secretion. Atropine likewise inhibits the secretion already induced by oleic acid, but only slightly affects the secretion induced by 2% Na oleate. The continuation of pancreatic activity induced by neutral fat even after atropine injection is to be attributed to the soaps produced during cleavage.

Influence of Neutral Fat and Its Components on the Gastro-  
Intestinal and Pancreatic Secretions

A. Z. Belina. Russky Vartch 11, 296 (1912), 11, 337 (1912)  
CA. 7:1899<sup>1</sup>

Neutral fats are the most specific stimulants of the secretion of pancreatic juice. After administration of fat the pancreatic juice contains its largest proportions of lipase. Fatty acids and soaps produce similar effects. Glycerol does not affect intestinal secretion.

The Effect of Margarine on the External Secretions of the Digestive Organs

S. Ryss and G. W. Borisow. Arch. Verdauungskrankh. 57, 184 (1935), Nutr. Abs. and Rev. 5, 104 (1936)

On dogs with various types of gastro-intestinal fistulae, the action of margarine on the pancreatic secretion was similar to that of other fats and oils.

The Physiology of Pancreatic Secretion

A. I. Smirnov. Arch. Ges. Physiol. 147, 234 (1912)  
CA. 7:1222<sup>1</sup>

In a dog the secretion of pancreatic juice occurs first 20-25 minutes after the introduction of fat into the duodenum where the contents of the duodenum are apparently neutral or alkaline. Simultaneously with the cleavage of the fat the secretion increases considerably. Such secretion is characterized by high N, solids, and ferments. A subcutaneous injection of 0.005 g. atropine at the time of greatest fat cleavage does not reduce the quantity of secretion but leads within 15 minutes to a reduction of the N and solids which then further continues.



## Influence of Fats and Soaps on the Secretory Function of the Pancreas

V. Studzinsky. Intern. Beitr. Path. Therap. 3, 287 (1912)

CA. 6:1175<sup>2</sup>

With dogs having duodenal and pancreatic fistulas, pure neutral fat causes no secretion of pancreatic juice, whereas commercial fats can cause secretion because of their content of free fatty acid. Pure fatty acids, such as oleic acid, are energetic stimulants of the pancreas, which explains why rancid fats irritate the mucous membrane of the intestine causing inflammation. Soaps in 1 - 10% solution act as stimulants. Atropine, previously injected, does not prevent secretion produced by the action of fatty acids or soaps. The secretion influenced by the fatty acid is identical with that influenced by soaps.

## Physiology of the Pancreas

A. Tonkisch. Arch. Ges. Physiol. (Pflügers) 206, 525 (1924)

CA. 19:1156<sup>7</sup>

Fat and milk stimulate the pancreas more than meat. Atropine inhibits the trophic action of fats on the pancreas. Oleic acid stimulates the secretion of pancreatic juice with a high N content, but after atropinization the N content is reduced. When oleic acid is introduced into the duodenum after separation from the stomach, the pancreatic juice has a low N content. The N content of the juice differs with different preparations of oleinate.

c.     Vitamins

The Effect of Irradiated Ergosterol on the Composition of  
Gastric and Pancreatic Juices

W. Bauer, A. Marble, S. J. Maddock and J. E. Wood. Am. J. Mod. Sc. 181, 399 (1931).

Following administration of irradiated ergosterol to 4 adults, pancreatic enzyme activity was depressed in 1 individual. The latter, however, may have been due to increased number of bowel movements of this subject. It had no effect on fixed base content of pancreatic juice. It did cause a fall in the chloride ion and a rise in the carbonate ion.

The Effect of Vitamin A on the External Secretion of the  
Pancreas

K. Herfort. Acta. Med. Scand. 96, 425 (1938), Nutr. Abs. and Rev. 9, 171 (1939)

Vitamin A was introduced into the duodenum of humans by means of a sound. The secretion of pancreatic juice elicited was greater than that obtained by similar administration of secretin or the solvent oil alone. The same action resulted when Vitamin A was given orally or parenterally.



Digestive Juico Secretion on Diets Containing Rice of Varying Degrees of Refinement. II. Pancreatic Secretion on Diets Containing Rice of Various Degrees of Refinement.

R. Masuko. Auchi Igakkai Zasshi 42, 1721 (1935), Nagoya J. Med. Sci. 10, 85 (1936). CA. 31:7484<sup>1</sup>

On dogs with pancreatic fistula the addition of vitamin B to polished rice accelerated secretion, lengthened its duration and caused a marked increase in volume and enzymic concentration. With half polished rice and germ containing rice vitamin B promoted secretion somewhat, but not with unpolished rice.

III. The Accelerating Action of Vitamin B on the Secretion of the Digestive Juices.

When vitamins B<sub>1</sub> and B<sub>2</sub> are separated the accelerating action on digestive secretion, present in unfractionated B, is no longer exhibited by either fraction.

Modification of the Hepato-Pancreatic Secretion by Administration of Vitamins A, B<sub>1</sub>, and C

P. Nicolesco et.al. Bull. Acad. Med. Roumanie 5, 121 (1940), Nutr. Abs. and Rev. 12, 117 (1942)

On individuals with various liver diseases, administration of Vitamin A by way of the duodenum increased the total output of pancreatic enzymes, Vitamin B<sub>1</sub> increased only the output of lipase and had no effect on trypsin output, and Vitamin C had no effect on the enzyme output.

Effects of Massive Doses of Vitamin D on the Histological  
Structure of the Glands of Internal Secretion

I. Nitzescu and S. Braliano. Compt. Rend. Soc. Biol. 121,  
1533 (1936). CA. 30:5623<sup>9</sup>

Changes in the pancreas are described.

Pancreatic and Intestinal Enzymes in Experimental Scurvy

G. Sunzeri. Problemi Nutriz. 3, 28 (1926); Ber. Ges.  
Physiol. Expt. Pharmacol. 38, 682 (1926). CA. 21:1834

Guinea pigs fed on a Vitamin-C free (Randoin) diet  
were killed shortly before death and their pancreas and  
intestinal mucosa were extracted with 0.1% NaCl. The  
only anomalies observed were: decrease of intestinal  
amylase by 2/3 and slight decrease in creptase content.

The Influence of Avitaminoses on Weights of Endocrine Glands

B. Surc. Endocrinology 23, 575 (1933). CA. 33:699<sup>3</sup>

In Vitamin A deficiency there is a 40% hypertrophy  
of the pancreas.

Enzymic Efficiency in .vitaminosis. II. Influence of Vitamin  
B. Deficiency on Efficiency of Pancreatic Lipase and Esterase.

Barnett Sure, M. C. Kik and Kathryn Sue Buchana. J. Biol.

Chem. 108, 27-33 (1935). CA. 29:1466<sup>1</sup>

In uncomplicated vitamin B and in vitamin B complex deficiency there is a pronounced decrease in pancreatic lipase activity which is due to specific vitamin deficiency. A deficiency of the vitamin B complex also reduces pancreatic esterase efficiency.

The Influence of Secretin and Antineuritic Vitamins on  
Pancreatic Secretion and Bile Flow

C. Voegtlin and C. N. Myers. J. Pharmacol. 13, 301 (1919)

CA. 14:1156<sup>4</sup>

Antineuritic vitamins from brewers' yeast on injection into dogs stimulated pancreatic and biliary secretions.



d. Mixed Diets and Comparative Studies

The Effect of Different Forms of Diet on the External Secretion of the Pancreas

L. Abramson. Acta. Med. Scand. 86, 478 (1935), Nutr. Abs. and Rev. 5, 982 (1936)

Normal human subjects lived on (Group A) the usual mixed diet of Sweden, and (Group B) a diet practically devoid of meat, fish and eggs but rich in milk and carbohydrate. On an empty stomach ether was injected into the duodenum by a tube to stimulate the pancreas, and the juice was collected. In Group B the diastase content was higher but the trypsin and lipase lower than in Group A. The differences were not statistically significant, although they are in keeping with previous work showing that Group B had hypochlorhydria.

The Action of Acid Solutions of Cane Sugar on the Secretion of Trypsinogen

B. P. Babkin and V. V. Savich. Russ. J. Physiol. 3, 143 (1921). Cl. 17:2146<sup>8</sup>

The pancreatic juice secreted on introduction of acid into the stomach is poorer in trypsinogen than that secreted on giving meat or carbohydrate. Addition of cane sugar to the acid increases the concentration of trypsinogen in the pancreatic juice. The increase does not depend on the act of feeding, since the acid sugar solution was injected directly through a gastric fistula.

The Content of Solids Contained in Pancreatic Juice Produced  
by Various Secretory Stimulants

B. P. Babkin and W. W. Sawitsch. Z. Physiol. Chem. 56, 321  
(1908). CA. 3:1414<sup>7</sup>

The character of the secretion was not dependent on the volume, but on the type of stimulation. The secretion set up by soaps is brought about by nervous influences. Experiments with milk, bread and meat indicated that secretion occasioned by milk is the result of the formation of soaps in the intestine. Meat and bread stimulate the pancreas by virtue of the high acidity of the gastric juice passing into the intestine, independent of nervous action.

Kliniske Studier over den Digestive Duodenalsaftschkretion.  
Samt et Bidrag til Spørgsmålet om den Exokrine Pankreas-  
Funktion ved Achylia Gastrica

Christiansen. Copenhagen. Levin & Munksgaards (1933)

(From McClure: Observations on the Physiology and Pathologic Physiology of External Pancreatic Functions. Rev. Gastroenterology 3, 1 (1936))

P. 5 & 6. No one kind of pure foodstuff stimulates the greatest concentration of its specific enzyme; however, the degrees of concentration of all types of pancreatic enzymes are related to the foodstuff fed.



External Pancreatic Fistula: Report of a Case with Physiologic Observations

M. W. Comfort, A. J. Osterberg and J. T. Priestley. Am. J. Dig. Dis. 10, 7 (1943)

The fasting secretion was low in volume, total bicarbonate and enzyme content. With gastric juice excluded pancreatic juice was stimulated very slightly by casein, glucose, and olive oil introduced through a duodenal tube. Given orally glucose and casein promoted vigorous secretions. Lipase was not stimulated to flow by olive oil given orally, but there was a slight increase in amylase. The type of secretory response did not appear to depend as much on the effect that food exerts directly on pancreatic secretion as on the effects of food on gastric secretion. Gastric contents (gastric secretion plus food) were a much more potent stimulant of pancreatic secretion than were foods alone. Meals low in fat and high in carbohydrate and protein stimulated a greater flow of all components of the pancreatic juice than did meals high in fat,

Physiology of the Pancreas

O. Cohnheim and Ph. Klee. Z. Physiol. Chem. 78, 463 (1912)  
CA. 7:122<sup>7</sup>

Various liquids were injected into the duodenum and the quantity of pancreatic juice obtained was compared with the normal. HCl is the strongest stimulant. The free acid is more effective than when combined with protein. Oil caused but a slight flow of pancreatic juice.

The Influence of Combinations of Basic Foodstuffs (containing chiefly proteins and carbohydrates) upon Gastric and Pancreatic Secretion

M. L. Eidlinova. Arch. sci, biol. (U.S.S.R.) 34, 113 (1934)  
CA. 28:5869<sup>7</sup>

Dogs were fed combinations of bread, potatoes, starch, meat and soy-meal and the pancreatic secretion collected by means of a Pavlov fistula. Equal weights of meat and potatoes or starch resulted in greater secretion than each of these alone. When the starch content was increased secretion was decreased; an increase in the potato content increased secretion. Soy-meal was less effective as a pancreatic stimulant than meat. Starch alone stimulates pancreatic secretion. The changes in acidity of the juice paralleled the volume changes while enzyme concentration did not.

The Action of Physiological Stimulants on Pancreatic Secretion

B. Goldstein. Arch. Verdauungs-Krank. 40, 56 (1927)  
CA. 21:2935<sup>6</sup>

After a high fat diet for about two weeks, 5 normal subjects showed an increase in lipase concentration, and an increase in concentration of protease when a high protein diet was given under the same conditions. Diastase did not show this adaptation to diet.

On the Mechanism of the Adaptation of Pancreatic Enzymes  
to Dietary Composition

M. J. Grossman, H. Greengard and A. C. Ivy. Am. J. Physiol.  
141, 38 (1944)

The young white rats used as experimental animals were sacrificed and the enzymes determined by analyzing the pancreatic tissue. Substitution of dextrose for corn starch in a balanced diet results in increased amylase content of the pancreatic tissue. Administration of protamine zinc insulin to rats fed a balanced diet causes a depression of amylase content. Substitution of casein hydrolyzate for casein in a balanced diet produces a depression of trypsin content.

The Effect of Dietary Composition on Pancreatic Enzymes

M. J. Grossman, H. Greengard and A. C. Ivy. Am. J. Physiol.  
138, 676 (1943)

Rats were fed various diets for 21 days and their pancreas was then removed and analyzed for enzymes. On a high carbohydrate diet there was pronounced increase in amylase with a decrease in trypsin. High protein diet resulted in increased trypsin and slight increase in lipase. High fat diet showed no alterations in trypsin or amylase. A diet high in fat and low in protein causes a repression of all pancreatic enzyme formation. The addition of 1% choline to such a diet increases uniformly the content of all enzymes.



The Control of the External Secretion of the Pancreas in Cats  
A. A. Harper and C. C. N. Vass. J. Physiol. 99, 415 (1941)

The juice was collected by means of a cannula in the pancreatic duct after normal saline, distilled water, 5% inulin solution, 5- 8% starch solutions or 5% casein solution were either injected into the stomach through a catheter passed down the esophagus or directly into the duodenum. In the latter instance the gastric juice was prevented from entering the duodenum.

The presence of foodstuffs in the stomach did not increase the enzyme output of the pancreas. As soon as the meal began to pass through the pylorus there was a sharp increase in enzyme output and of total juice. The passage of a casein or starch meal brought about in each case a parallel increase in the amount of trypsinogen and amylase. All the substances caused an increase in enzyme output when injected into the duodenum. The fact that water and a non-utilizable substance like inulin caused an increase in enzyme output was thought possibly due to the distension of the duodenum. But experiments using a balloon in the duodenum showed that it was the substances that exerted the stimulatory effect.

The above effects occurred when all the extrinsic nerves to the small intestine had been cut.

### The Buffer Capacity of Pancreatic Juice

M. T. Hoerner. Am. J. Dig. Dis. 2, 300 (1935)

From dogs with pancreatic fistulas the juice was collected every half hour during fasting and after test meals. Protein diets stimulated the flow more than carbohydrates or fat. The buffering capacity of the juice reached its maximum one to three hours after ingestion of food and gradually diminished as the acidity in the duodenum decreased. The secretion was always alkaline and even possessed slight buffering power while fasting.

### Physiology of External Pancreatic Secretion. VI. Further Studies.

A. C. Ivy. J. A. M. A. 39, 1030 (1927)

A review is given of the mechanisms of pancreatic secretion. The pancreatic secretory response of dogs to meat and olive oil under various conditions is given in volume per 15 minutes, over a period 4 - 5 hours. The amount of juice secreted in response to meat was about three times that elicited by olive oil. Enzyme analysis of the juice is not reported.

The Influence of a Diet of Milk and Bread upon the Activity of the Pancreas

U. M. Joblonski. Arch. d. Sci. Biolog. 4, 377 (1894)

(From The Work of the Digestive Glands, I. P. Pavlov, 1910)

P. 45 The proteolytic power of the pancreatic juice of a dog fed on meat was very high, but when placed on a milk and bread diet it decreased continuously over a period of time.

"When, under the influence of a given diet, a particular condition of the pancreatic activity had been established in our experimental animals, we were able, by altering the feeding, to reverse it several times in one and the same animal."

P. 46 "Although our laboratory dogs live and are fed under the same conditions, nevertheless the pancreatic juice of the different animals often differs very essentially in the amount of ferment. A change of diet in the case of one dog may very soon manifest itself in altered properties of the juice, while, in another, the remoulding of the pancreas takes place in the slowest manner. In such cases as the latter, an abrupt transition from one regime to another may often produce serious illness."



A Study of External Pancreatic Secretion in Man

B. Kogut, M. J. Matzner and A. E. Sobel. J. Clin. Inv. 15  
393 (1936)

In a woman with a partial external pancreatic fistula, an increased rate of secretion was observed after the ingestion of food. Tests were insufficient to make any conclusions as to the effect of different types of food on secretion. Enzyme analysis was not done, but the various chemical components were analysed quantitatively.

Experimental Criticism of the Doctrine of the Adaptation of the Digestive Enzymes

I. Erepsin of the pancreatic juice collected after varied feeding.

U. Lombroso. Intern. Beitr. Path. Therap. 3, 333 (1912)  
CA. 6:1174

II. Lipase of the pancreatic juice collected after varied feeding.

R. Bompiani. Ibid. 347

III. Amylase of the pancreatic juice collected after varied feeding.

T. Rinaldini. Ibid. 356

As a result of their work they conclude that there is no special production of specific enzymes in pancreatic juice to meet the immediate needs of different foods. The variations in enzyme output are ascribed to other sources than the ingested food.

The Dynamics of Internal Secretions. III. Internal and External Secretions.

E. S. London. Arch. Ges. Physiol. (Pflugers) 228, 531 (1931)  
CA. 27:2191<sup>8</sup>

The maximum output of pancreatic juice after the ingestion of meat is 2 hours, after bread 2 hours, and after milk 3 hours, while the maximum output of insulin occurs at the 4th, 5th and 6th hours respectively.

The External Secretory Function of the Human Pancreas

J. M. McCaughan, B. L. Sinner and C. J. Sullivan. Arch. Int. Med. 61, 739 (1938)

Physiologic observations on the external secretory function of the human pancreas were made on a patient in whom a pancreatic fistula developed after a gastric resection. A rise in the secretory rate of juice followed the administration of secretin, a mixed meal, water, hydrochloric acid, beef broth, dextrose, olive oil, peptone, coffee, mech-olyl and physostigmine. A fall occurred after the administration of sodium bicarbonate, bile salts, magnesium sulfate, atropine, epinephrine and histamine. The total base was elevated after the administration of secretin, sodium bicarbonate and coffee, and was depressed after administration of a mixed meal, beef broth, dextrose, bile salts, physostigmine, epinephrine and histamine. There was no significant change after administration of hydrochloric acid, peptone and magnesium sulfate.

Effects of Administration of Pure Foodstuffs and Inorganic Substances on External Secretary Activities of the Liver, Pancreas and Stomach

C. W. McClure, M. E. Huntsinger and A. T. Fernald. Am. J. Physiol. 107, 94 (1934)

In normal young men, cottonseed oil, peptone,  $\text{MgSO}_4$ , HCl, and dextrose stimulated the secretion of concentrated pancreatic juice in the order given. The secretion of bile was affected in the same manner, except that  $\text{MgSO}_4$  and HCl were reversed in potency.

Studies in Pancreatic Function: Enzyme Concentration of Duodenal Contents after the Ingestion of Pure Foodstuffs and Food Mixtures by Normal Men

C. W. McClure and A. S. Wetmore. Bost. Med. & Surg. J. 187, 882 (1922)

The juice collected through a gastroduodenal tube was greater after the ingestion of food than during fasting secretion. Lipolytic activity of the juice was greatest after the ingestion of olive oil; less after protein and least after carbohydrate. Duodenal contents obtained after the ingestion of olive oil showed greater degrees of all types of enzymatic activities than after protein. After the appearance of food substances in the duodenum there was a latent period before the flow of enzymes and bile began.



Physical Characters and Enzymatic Activities of Duodenal Contents

C. W. McClure, A. S. Wetmore and L. Reynolds. J. A. M. A. 77, 1468 (1921)

The findings on 15 normal young men are given after they had ingested test meals. The enzymic activity of the juice secreted after the ingestion of cream, cottage cheese and milk meals were considered as standard because of the uniformity of enzyme response to them. After water meals, during fasting and occasionally after starch and lactose meals the output of enzymes was lower.

On the so-called Adaptation of the Pancreas

V. Michelson. Archiv. f. Verdauungskrankheiten 51, 73 (1932)

A review article covering the relationship of different types of food to pancreatic enzyme output.

According to Poljak the administration of diets high in carbohydrate, proteins or fat did not elicit any change in the concentration of enzymes of the pancreatic juice.

In dogs, various workers have shown an adaptation of enzyme output to diet, although some workers showed that fat didn't elicit a specific response. This latter observation was ascribed to the fact that dogs usually have little fat in their diet.

(This is one of the best reviews that has been found on this particular aspect of the work.)

Some Observations of the Pancreatic Secretion in a Dog

T. Muto. Tohoku J. Exptl. Med. 31, 479 (1937). CA. 32:6311<sup>5</sup>

A dog with a permanent pancreatic fistula was fed a mixture of rice and fish foods with beef, bread and milk in amounts equivalent to  $1/3$  of the calories required for maintenance of the normal metabolism. Carbohydrate-rich diets increased pancreatic secretion but reduced gastric secretion. The pancreatic juice contained more trypsin after a protein-rich diet and more amylase after a carbohydrate-rich diet. Lipase was unaltered. Alkali was reduced during the non-digestive period.

The Relationship of Pancreatic Enzymes to Food Allergy

A. W. Oelgoetz, P. A. Oelgoetz and J. W. Wittking. Am. J. Dig. Dis. 1, 730 (1934), Ibid. 2, 422 (1935), Ibid. 3, 199 (1936), Med. Rec. 143, 20 (1936), Ibid. 150, 276 (1939)

The following hypothesis is set forth in all the papers: The amount of enzymes secreted by the normal functioning pancreas is in excess of that required for digestion in the intestine. The 'surplus' of enzymes is absorbed and enters the blood. Food is absorbed in various degrees of digestion--from protein to amino-acid--and digestion is continued in the blood by virtue of the circulating enzymes. In instances of pancreatic insufficiency the enzyme output may be just enough to take care of intestinal requirements

and none, or a very slight amount, enters the blood. Therefore the proteins, metaproteins, etc., in the blood are not digested and the animal becomes sensitive to foods. Further ingestion of food while in this condition causes an allergic reaction to occur. To counteract this the administration of less food, or of dry pancreatic enzymes is suggested.

A test is described to quickly and easily measure blood enzyme levels. A starch-iodine mixture is used and the serum is allowed to act on it. This measures the amylase, but the blood enzymes always follow a parallel concentration and therefore it is considered an index of the total blood enzyme content.

Pancreatic Function. V. The secretory mechanism of the digestive juices.

S. Okada, et al. Arch. Internal Med. 45, 783 (1930)  
CA. 24:3816<sup>3</sup>

Sugar shows an inhibitory action on the secretory center of gastric, pancreatic and biliary secretions. Amino acids and fats stimulate these secretions.

The Influence of Physiological Stimuli on Pancreatic Function

N. N. Poljak. Deutsch. Arch. f. Klin. Med. 170, 574 (1931),  
Nutr. Abs. and Rev. 1, 118 (1931)

The effect of test meals, of cane sugar, starch, egg-white, peptone and oils, introduced into the duodenum, was



tried on the secretion and ferment activity of the pancreatic juice in 13 persons. None of the meals excited a specific secretion of juice rich in the appropriate ferment.

Effects of Feeding Stuffs on the Pancreatic Function of Calves

n. Popov, E. Shmakova and V. Kuynetsova. J. Physiol. (USSR) 17, 52 (1934). CA. 31:7476<sup>2</sup>

Sunflower silage increases the quantity and alkalinity of pancreatic juice. Straw foods have the reverse effects.

The Work of the Pancreatic Secretion

A. A. Walther. Arch. d. Sci. Biol. 8, (1899)

(From The Work of the Digestive Glands, I. P. Pavlov, 1910)

P. 42 In an experiment using diets of milk, bread and meat, the quantity of juice secreted, the duration of secretion, % dry solids, % ash, % organic substances, % N, and alkalinity of ash, of the juice were determined. From these results it is seen that, as regards the total quantity of juice, the duration, of its outflow, the percentage of total solids, and, in particular, the percentage of organic solids, there are striking differences manifested in the secretion poured out for the different foods. The quantity of juice corresponds neither to the total weight of the food, the amount of solids which it contains, nor to the quantity of protein in the different varieties given. It is related to the physical and chemical

properties of the food as a whole. The percentage of organic solids which runs parallel with the quantity of ferment is seen in "milk juice" to be nearly double as high as that in "bread juice" and nearly 3 times as great as that in "meat juice". The percentage of ash and the degree of alkalinity are also very different in the 3 cases. If the total quantities of organic solids be calculated for the foregoing diets, it will be seen that milk and flesh receive almost equal amounts, while bread receives double that of either.

### SECTION III

#### EFFECT OF FASTING AND ENVIRONMENT ON PANCREATIC SECRETION



The Influence of Complete and Prolonged Fasting on the Secreting Power of the Pancreas, the Proteolytic Activity of the Pancreatic Juice, and on the Content in Secretin and Enterokinase of the Small Intestine

A. G. Barbera. Arch. Fisiol. 4, 413 (1907). CA. 1:2719<sup>5</sup>

In dogs which have fasted until they lost 45% of their weight, the pancreatic juice is the same as that in fed animals.

A Difference in Effect of Distilled and of Isotonic Solution in Intestine and Pancreatic Secretion

J. O. Crider and J. E. Thomas. Proc. Soc. Exp. Biol. & Med. 44, 299 (1940)

Distilled water in the intestine causes pancreatic secretion; isotonic solutions of inert substances in water do not.

The Activity of the Pancreatic Function under the Influence of Copious Water Drinking with Meals

P. B. Hawk. Am. J. Physiol. 27, XXVI (1910)

The activity of the pancreatic function as measured by the fecal amylase was found to be greatly facilitated when additional volumes of H<sub>2</sub>O ranging from 1500-4000 cc. were daily ingested at meals by normal men on a uniform diet.

Exhaustion of the Pancreas during Prolonged Activity.

I. Changes in the Buffer Constituents of Pancreatic Juice.

A. G. Kantser. Med. Exptl. (Ukraine) No. 6, 85 (1936)

CA. 31:2266<sup>5</sup>

In experiments on dogs prolonged pancreatic activity resulted in a decrease in the pH, titratable alkalinity, and the buffer capacity of the juice. The latter occurred mainly at the expense of N and P constituents.

Changes in the Rate of Secretion and Concentration of the Pancreatic Juice during Prolonged Activity of the Gland

A. G. Kantser. Med. Exptl. (Ukraine) No. 8, 103 (1936)

CA. 31:2266<sup>6</sup>

During prolonged activity of the pancreas, the rate of secretion gradually decreased while the concentration of the dry residue increased (mainly the organic constituents, the inorganic constituents remaining more or less constant).

Effect of Body Temperature on Pancreatic Secretion

S. L. Osborne and H. Graengard. Am. J. Physiol. 133, P404 (1941)

Raising the body temperature resulted in an increased flow of pancreatic juice up to 7 times the original rate, and lowering of the temperature operated to cause complete cessation of secretion.

The Effect of Dehydration on the Pancreatic and Intestinal Enzymes

J. R. Ross and H. M. Shaw. J. Biol. Chem. 104, 131 (1934)  
CA. 28:1396<sup>9</sup>

Young rats fed a normal diet but given no water, and placed in an incubator for alternate 12 hour periods for 4 days, showed a decrease in the production of pancreatic and intestinal enzymes.

Exocrine Pancreatic Secretion in the Fasting Dog

V. B. Scott, J. S. Graham, D. H. McCartney. Am. J. Dig. Dis. 7, 1 (1940)

The flow of pancreatic juice in fasting dogs showed marked irregularities, being greater in Dragstedt and Inlow than in the Elman and McCaughan fistulae. Bilateral intrathoracic vagotomy did not alter these irregularities.

The Relation of Fasting External Pancreatic Secretion to Hunger

V. B. Scott, C. C. Scott, and H. J. Bugol. Am. J. Physiol. 131, 60 (1940)

In gastrotomized animals with cannulated pancreatic ducts, a temporal correlation exists between the periodic motility of the stomach (hunger) and the external secretion of the pancreas, but this only showed up in 50% of the records. However, when both fasting pancreatic secretion and



hunger periods were present the correlation of this activity was 83%. Periodic activity of the stomach and pancreas occurred at irregular intervals; fasting pancreatic secretion can occur in complete absence of hunger contractions and can fail to appear with the onset of powerful hunger contractions.

#### SECTION IV

#### THE EFFECT OF SUBSTANCES OTHER THAN FOOD ON THE SECRETION OF PANCREATIC JUICE

- a. Insulin and Blood Sugar
- b. Acids, Alkali and Secretin
- c. Bile and Bile Derivatives
- d. Miscellaneous Substances

a. Insulin and Blood Sugar



Blood Sugar Concentration and the External Secretion of the  
Pancreatic Gland

B. P. Babkin. J. A. M. A. 105, 1659 (1935)

A review of the work done. Hyperglycemia always increases the output of enzymes from the acinous cells and in certain cases increases the volume of the secretion. Hypoglycemia produced by the administration of insulin lowers the concentration of enzymes in the pancreatic juice. After section of the vagus this effect disappears. The conflicting results obtained with humans are ascribed to the methods of recovering the juice.

The External and Internal Secretion of the Pancreas

H. Baer. Klin. Wochschr. 2, 1459 (1923). Ch. 18:537<sup>9</sup>

The secretion of pancreatic juice is increased when ether is introduced into the duodenum, and blood sugar is reduced at the same time indicating increase of internal secretion. Glucose given intravenously leads to an increase of steapsin and trypsin, but a decrease of diastase.

Blood-Sugar Concentration and Pancreatic Secretion in the  
Rabbit

S. G. Baxter. Quart. J. Exptl. Physiol. 21, 355 (1932)

Ch. 26:3550<sup>8</sup>

Insulin hypoglycemia caused a diminished output of enzymes by the pancreatic gland in a rabbit having vagi intact

and spontaneously secreting pancreatic juice. This phenomenon was not observed if the vagi had been cut. When the secretion has been arrested by hypoglycemia it may be restored by intravenous injection of hypertonic glucose solution.

Relationship between the Internal and External Secretion of the Pancreas

G. Dousch and E. Drost. Klin. Wochschr. 6, 2180 (1927)  
Ch. 22:625<sup>4</sup>

Impairment of the internal secretory function of the pancreas as this occurs in the diabetic, has no effect upon the secretion or composition of the digestive fluid.

The Action of Hormones on the Secretion of the Digestive Enzymes. V. Influence of Insulin on the Secretion of Pancreatic Enzymes.

R. Ferrari. Arch. Fisiol. 35, 145 (1935). Ch. 30:4907<sup>8</sup>

Dogs were treated with insulin and the pancreatic secretion was investigated during hypoglycemia. The amylolytic power was decreased 10-20 times; the lipolytic and proteolytic powers increased 2-6 times. The action is supposedly not due to hypoglycemia, as artificial hyperglycemia has no influence on the enzyme content. Concludes that insulin acts directly on the pancreatic tissue.

Action of Insulin on the External Secretion of the Pancreas  
in the Case of Pancreatic Fistula

F. Fonseca and C. Trincão. Compt. Rend. Soc. Biol. 99,  
1532 (1928). Ch. 23:1441<sup>5</sup>

Experiments with human subjects showed that insulin increased quantitatively the external secretion of the pancreas when given with a mixed diet, but does not affect the external pancreatic secretion under fasting conditions.

Action of Certain Drugs on the External Secretion of the  
Human Pancreas

Ibid 1533

Tests with a patient having a pancreatic fistula proved that odor or sight of food, pituitrin, atropine, pilocarpine and ergotamine increased the flow from the fistula. Pituitrin, atropine and ergotamine decreased the quantity of enzymes in the juice, while pilocarpine increased the enzymes. Adrenalin decreased both the flow and the enzymes, while ephedrine and ephedrine diminished the secretion without changing the enzymes.



Effect of Intra-Duodenal Injection of Acid on the Internal Secretion of the Pancreas

J. Freud and Sadi-Nezim. Compt. Rend. S. c. Biol. 95, 571 (1926). Ch. 22:458<sup>4</sup>

Injection of 0.5% HCl into the duodenum of dogs anaesthetized with chloral or into the stomach of non-anaesthetized dogs causes a diminution of the blood sugar which begins 15-30 minutes after the injection and lasts for 1-2 hours, indicating that substance bringing about the secretion of the pancreatic juice also cause production of insulin.

External Pancreatic Secretion and the Discharge of Bile During Hypoglycemia Following Intravenous Administration of Insulin

A. R. Frisk and G. Wolin. Acta. Med. Scand. 91, 170 (1937) Ch. 30:2291<sup>8</sup>

There was a small increase in duodenal contents, a slight increase in the bicarbonate concentration, and a marked increase in diastase. The flow of bile was also stimulated.

Relation Between the Blood-Sugar Concentration and the  
Exocrine Function of the Pancreas

C. O. Hobb. Arch. Intern. Pharmacodynamic 52, 33 (1935)  
Ch. 30:6448<sup>5</sup>

The concentration of blood sugar affects the amount of enzyme secreted by the pancreas. Intravenous injection of glucose causes increased enzyme secretion but NaCl or  $\text{NaHCO}_3$  does not. Atropine inhibits the effect so the increased lipase activity is probably due to the effect of the blood sugar on the parasympathetic nerves. The direct addition of glucose to the pancreatic juice does not increase its lipolytic activity.

Variations in Pancreatic Secretion during Hyperglucemia  
Resulting from Intravenous Injection of Glucose

J. LaBarre and P. Destree. Compt. Rend. Soc. Biol. 105,  
35 (1930). Ch. 26:3831<sup>4</sup>

Hyperglucemia stimulates the higher nervous system, leading to vigorous pancreatic secretion.

Insulin and the External Secretion of the Pancreas

J. LaBarre and P. Destree. Compt. Rend. Soc. Biol. 98,  
1237 (1928). Ch. 22:2790<sup>4</sup>

The injection of insulin causes a diminution in the output of pancreatic juice especially marked at the moment

of the greatest lowering of the glucemia. Lipase, trypsin and amylase are diminished at the same time.

Stimulating Action of Intravenous Injections of Dextrose on the External Secretion of the Pancreas

J. LeBarre and P. Destree. Compt. Rend. Soc. Biol. 98, 1240 (1928). CA. 22:2790<sup>5</sup>

Injection of hypertonic glucose solutions causes an increase in the pancreatic secretion and the enzyme content of the secretion.

The Effect of Insulin Therapy on Pancreatic Enzymes in Malnutrition

C. A. Lueders and M. E. Watson. Arch. Int. Med. 49, 330 (1932)

Injections of insulin twice daily in a group of patients with malnutrition, produced measurable increase in the concentration of pancreatic enzymes recovered from the duodenum during fasting. Studies of the stool before and following insulin therapy showed a direct parallel between the more complete digestion and assimilation of food elements and the increased concentration of pancreatic enzymes.



### Pancreatic Function

Okada, et. al. Arch. Int. Med. 43, 446 (1929)

With human subjects insulin stimulates gastric, biliary and pancreatic secretion; epinephrine and ephedrine inhibits it. When dextrose is introduced into the duodenum it brings about an initial increase of pancreatic juice; the hyperglycemia resulting after it is absorbed, through, stops the flow of juice almost entirely.

### Pancreatic Activity in Diabetes Mellitus

S. Okada, et.al. Proc. Imp. Acad. (Japan) 4, 134 (1928)

Ch. 22:4638<sup>3</sup>

The disturbance of pancreatic function manifests itself in the decrease of enzymic activity or of the amount of juice, or of both, the greatest alteration in enzymic efficiency and activity being in the proteolytic and lipolytic enzymes. There may be disturbances either in the internal or of the external secretion, or of both, the severity of the diabetes not necessarily running parallel to the degree of disturbance in the external secretion.

### The External Secretion of the Pancreas and Diabetes Mellitus

H. M. Pollard, L. Miller and W. A. Brewer. Am. J. Dig. Dis. 10, 20 (1943)

In a clinical study using the secretin test there were diminutions in volume of secretion, total secretion of bicar-

bonate, and the enzymes amylase and trypsin. These findings are correlated only with the duration of the disease and not with the age of the patient, the severity of the disease, the presence or absence of acidosis, the amount of insulin required or the diet.

The Relation of External Pancreatic Secretion to Variations in Blood Sugar

V. B. Scott, N. J. Collignon, H. J. Bugel and G. C. Johnson.  
Am. J. Physiol. 134, 208 (1941)

Insulin hypoglucomia increases the volume of pancreatic juice secreted by unanaesthetized dogs with permanent pancreatic fistulas. Intravenous glucose temporarily inhibits the pancreatic secretion which appears spontaneously or in response to insulin. Exclusion of the gastric juice from the duodenum abolishes the rapid pancreatic secretion of insulin hypoglucomia. Spontaneous variations in the volume of the fasting pancreatic secretion and gastric motility are unrelated to the fluctuations in blood sugar.

Diabetes and External Secretion of the Pancreas

T. B. van Steenis. Nederland. Tijdschr. Geneeskunde 78, II, 1529-36 (1934). CA. 29;212<sup>1</sup>

Records are given showing that the external secretion of the pancreas is often disturbed in diabetes.

b. Acids, Alkali and Secretin



The Effect of Changes in the Reaction of the Blood on  
Pancreatic Secretion

J. A. Archawsky. Arch. Ges. Physiol. (Pflugers) 224, 128  
(1930). CA. 24:4543<sup>9</sup>

The pH and CO<sub>2</sub> content of the blood are related to  
the pancreatic secretion.

The Composition of Pancreatic Juice and Blood Serum as  
Influenced by the Injection of Acid and Base

E. G. Ball. J. Biol. Chem. 86, 433 (1930). CA. 24:3819<sup>1</sup>

The pH of pancreatic juice varies with its rate of  
flow, the juice being more alkaline when secreted rapidly.  
The sum of (HCO<sub>3</sub><sup>-</sup>) and (Cl<sup>-</sup>) is nearly constant regardless  
of the rate of flow. Intravenously injected HCl does not  
affect the pH greatly. Intravenously injected Na<sub>2</sub> CO<sub>3</sub> in-  
creases the (HCO<sub>3</sub><sup>-</sup>) and (N<sub>a</sub><sup>-</sup>) of the juice but does not  
affect its pH.

A Disturbance of Pancreatic Secretion in Connection with  
the Clinical Observation of a Case of Continued Pancreatic  
Super-Secretion

Bickel. Deut. Med. Wochschr. 34, 2111 (1908). CA. 3:661<sup>6</sup>

The amount of secretion at various times are tabu-  
lated. The flow was reduced on giving NaHCO<sub>3</sub> or opium.

### The Juices of Pancreatic Hypersecretion

C. Fleig. Compt. Rend. Soc. Biol. 70, 16 (1911). CA.5:1293<sup>8</sup>

Hypersecretion from the pancreas obtained by fistulas and injection of HCl showed a lipolytic power below normal. This is due to changed viscosity and alkalinity rather than to any change in lipase content.

### Acid-Base Composition of Pancreatic Juice and Bile

J. L. Gamble and M. A. McIver. J. Exp. Med. 48, 849 (1928)

The juice was obtained from a human with a pancreatic fistula and from dogs with duodenal fistulas. Pancreatic juice contains fixed base at approximately the concentration found in the blood plasma. Chloride ion is present in concentration varying from one-fourth to one-half the fixed base value and the remainder of the acid equivalence is composed of bicarbonate ion. Fixed base being a nearly stationary factor, variation of bicarbonate and thereby of alkalinity is referable to change in the concentration of chloride ion.

### The Effect of Hydrogen Ions of Carbonated Water on Pancreatic Secretion

F. Kmietowicz. Compt. Rend. Soc. Biol. 89, 493 (1923)

CA. 18:855<sup>1</sup>

Pancreatic juice is increased following the introduction of carbonated mineral water. The secretory principle

in mineral water containing  $\text{CO}_2$  is the  $\text{H}$  ion of the carbonic acid. After boiling such water loses its effectiveness.

Pancreatic Secretion in Disturbed Gastric Secretion

S. Okada, et.al. Proc. Imp. Acad. Tokyo 4, 423 (1928)

CA. 23:430<sup>6</sup>

The pancreatic secretion is not necessarily disturbed by disturbed gastric secretion. In some cases it is increased. The presence of  $\text{HCl}$  is not necessary to stimulate normal pancreatic secretory activity.

The Secretory Activity of the Pancreas as Influenced by Hydrochloric Acid and Intestinal Extracts (so-called "Secretin")

L. Popielski: Arch. Ges. Physiol. (Pflügers) 120, 451 (1907)

CA. 2:2099<sup>3</sup>

The Characters of the Secretory Activity of the Pancreas Under the Influence of the Hydrochloric Acid and of the Intestinal Extracts

Ibid. 121, 239 (1908). CA. 2:3000<sup>3</sup>

Two extensive articles, the main purpose of which is to criticize Bayliss and Starlings' secretin hypothesis. Contains the results of experiments dealing with the effect of many types of substances on pancreatic secretion.



The Dependence of the Secretory Products of the Digestive Glands on the nature of the Stimulus Inciting Them. The Effect of the Acidity of Fluids Introduced into the Duodenum on the pH of the Pancreatic Secretion

N. A. Popov and A. A. Kudryashev. Arch. Ges. Physiol. (Pflugers) 224, 66 (1930). CA. 24:4543<sup>7</sup>

The introduction of 0.1% HCl into the duodenum of a decerebrate dog resulted in the production of pancreatic secretion of greater acidity than that which followed the introduction of a 0.5 to 1.0% HCl solution.

A Quantitative Study of Acid in the Intestine as a Stimulus for the Pancreas

J. E. Thomas and J. O. Crider. Am. J. Physiol. 131, 349 (1940)

From dogs with gastric and duodenal fistulas pancreatic juice was collected after adding various buffer solutions to the intestine. The pH threshold for the stimulation of pancreatic secretion was near pH 5.0. The practical acid threshold for causing a significant amount of secretion in the dog digesting raw meat was estimated to be near pH 4.0.

Specific Gravity and Total Nitrogen of Pancreatic Juice Secreted in Response to Various Stimuli

J. E. Thomas and J. O. Crider. Am. J. Physiol. 140, 574 (1933)

Various stimuli were injected into the intestines of unanaesthetized dogs provided with gastric and duodenal

fistulas. The specific gravity and total nitrogen of the juice was noted. Peptone causes the most concentrated secretion, soap a less concentrated one, and HCl the most dilute. The latter secretion was similar to that caused by intravenous administration of secretin.

Influence of Alkali on the Function of the Pancreatic Glands

V. N. Vorobyev. Zentr. Physiol. 28, 617 (1914). CA.9:104<sup>6</sup>

Intravenous injection of alkaline salts of Na, K, Li, Ca,  $\text{NH}_4$  and Mg in dogs caused an increase in flow of pancreatic juice, the more soluble ones causing a rapid flow of short duration and vice versa. Alkaline solutions cause an increased alkalinity of the juice and a lowered ferment content.

Changes in the Duodenal Juices Effected by the Introduction of Various Substances

M. Wichert and W. Dworjetz. Arch. Verdauungs-Krankh. 34, 158 (1925). CA. 19:1732

The introduction of HCl into the duodenum calls forth increased trypsin secretion; oil effects an increase in the lipase and ether causes marked secretion of the pancreatic juice.

The Influence of Sodium Hydrogen Carbonate on the Pancreatic Secretion

E. Wilbrand. Munch. Med. Wochschr. 61, 1437 (1914)

CA. 9:223<sup>7</sup>

On dogs with duodenal fistula  $\text{NaHCO}_3$  per os diminishes the pancreatic secretion, more so when given in solution than in substance.

Heat Production in the Pancreas. III. The inhibitory effect of saline on the HCl-pancreatic secretion.

N. Yoshii. Japan J. Med. Sci. III Biophys. 4, 409 (1937)

CA. 32:9262<sup>4</sup>

With anaesthetized dogs the intravenous or intraduodenal injection of physiological saline or of a 15% salt solution decreased the secretion of pancreatic juice in response to the introduction of HCl into the duodenum. There was no effect on the blood pressure or on the temperature of the pancreas.

Continuous Pancreatic Secretion

T. F. Zucker, P. G. Newburger and B. N. Berg. Am. J.

Physiol. 102, 193 (1932)

In a dog with cannulated pancreas the secretion is continuous, but food or the injection of secretin temporarily increases the rate of flow. Anaesthesia may completely inhibit the flow of pancreatic juice. Ether increases the amylase level of the blood.



c. File and File Derivatives

The Relation of Bile to the Secretion of Pancreatic Juice

L. R. Dragstedt and R. A. Woodbury. Am. J. Physiol. 107, 584 (1934)

Concludes that in the dog the presence of bile in the duodenum cannot be considered essential for the secretion of pancreatic juice.

Bile Salts and Secretin as Chologogs

J. Mellanby. J. Physiol. 64, 351 (1928). CA. 22:3206<sup>2</sup>

Bile, placed in the duodenum, stimulated the secretion of both pancreatic juice and bile; placed in the ileum it stimulated the liver and not the pancreas; injected into the blood bile salts stimulated bile flow and had no effect on pancreatic secretion.

The Secretion of Pancreatic Juice

J. Mellanby. J. Physiol. 61, 419 (1928)

Cholic acid is the active substance in bile stimulating the flow of pancreatic juice, but its activity is modified by its association with taurine and glycine, and the presence of mucin in the bile.

The Effect of Bile in the Intestine on the Secretion of Pancreatic Juice

J. E. Thomas and J. O. Crider. Am. J. Physiol. 138, 548 (1943)

In normal unanaesthetized dogs provided with gastric and duodenal fistulas the injection of ox bile or dog bile

into the intestine does not increase the rate of secretion of pancreatic juice. The amount of pancreatic juice secreted in response to the presence of peptone, soap or HCl in the intestine is less when bile is also present than when it is absent from the intestine.

Experimental Study on the Mutual Relation Between the Pancreatic and Hepatic Functions

T. Yuasa. Japan. J. Gastroenterol. 8, 187 (1936)

CA. 31:148<sup>4</sup>

In hepatic disturbance the pancreatic juice increases while the quantity of enzymes remains quite constant. Bilirubin, cholesterol and bile acid salts can be injected into the blood without affecting the secretion of the pancreas.



d. Miscellaneous Substances

The Parallel Concentration of Enzymes in the Pancreatic Juice

S. G. Baxter, Am. J. Dig. Dis. 2, 108 (1935)

The pancreatic duct of anesthetized rabbits was cannulated and the juice collected. After stimulating the flow with pilorcarpin the enzymes of the juice showed a parallel increase with the increased flow of juice.

The Effect of Magnesium Chloride of Mineral Waters on the Secretion of Glands Emptying into the Intestine

P. Carnot and H. Gaehlinger, Compt. Rend. Soc. Biol, 88, 1129 (1923). CA. 18:123<sup>8</sup>

Experiments with dogs and humans shows that isotonic solutions of  $MgCl_2$  either per rectum, subcutaneously or through the duodenum stimulate the activity of the liver, pancreas and intestinal glands, the secretion also possessing increased enzymic activity. Similar results were obtained with  $MgSO_4$ , but much thick bile results.  $Na_2SO_4$  produces the same effect when introduced into the duodenum, but no effect subcutaneously.

The Histological Change in the Endocrine and Other Organs  
after the Administration of Cayenne by Mouth to Rabbits

C. Y. Choi and Y. G. Lee. Korean Med. J. 7, 77 (1937)

CA. 32:4227<sup>1</sup>

Hyperfunction of the pancreas was shown in histological picture at the initial stage of administration, but by continuous feeding hypofunction was gradually exhibited.

The Effect of Barbiturates on Digestive Secretion

R. J. Coffey and R. Koppanyi. Am. J. Dig. Dis. 7, 21 (1940)

Barbiturates in large hypnotic and anaesthetic doses produce a reduction of the gastric and pancreatic secretions, with a prompt return to normal flow after hypnotic doses, and a delayed return after anesthetic doses.

Pancreatic Secretion in Man After Administration of Different Stimulants: A Comparative Study

M. W. Comfort and A. E. Osterberg. Am. J. Dig. Dis. 8, 1 (1941)

. Administration of vitamine A and starch did not produce a measurable stimulation of the fractions of the duodenal contents. Mecholyl stimulated various fractions of duodenal contents more uniformly and potently than casein, fat and prostigmine methylsulfate. Secretin is stimulant of choice for study of secretion of fluid and bicarbonate; secretin plus mecholyl chloride effected greatest secretion of all fractions of duodenal contents.

The Effect of Ephedrine on Pancreatic Secretion

C. B. Craft. Surgery 4, 64 (1938). CA. 32:7571<sup>8</sup>

Ephedrine produced a definite decrease of secretion of pancreatic juice in dogs.

Action of Formaldehyde Injected into the Intestine on Pancreatic Secretion

C. Delezenne and E. Pozerski. Compt. Rend. Soc. Biol. 78, 23 (1915). CA. 10:2374<sup>1</sup>

In dilute concentrations formaldehyde stimulated the flow of pancreatic juice.

The Effect of Phlorhizin upon Pancreatic Secretion

L. Dunner and H. Blume. Klin. Wochschr. 10, 445 (1931) CA. 25:4054<sup>2</sup>

The intramuscular injection of phlorhizin into normal human subjects usually causes a  $1\frac{1}{2}$  - 2 fold increase in duodenal secretion. The enzyme content of the fluid is markedly increased, particularly with respect to trypsin and diastase. With certain pathological conditions the effect was not observed.



The Influence of Magnesium Sulfate on the Secretory Activity of the Digestive Glands

W. H. Gantt and G. V. Volborth. Am. J. Med. Sci. 179, 375 (1930). CA. 25:147<sup>2</sup>

There was a slight increase in pancreatic juice after giving  $\text{MgSO}_4$  through a stomach tube.

The Enzyme Content of Pancreatic Secretion Following Various Stimulants

H. Greengard, M. J. Grossman, R. A. Roback and A. C. Ivy. Am. J. Physiol. 141, 509 (1944)

Pancreatic juice was collected from anaesthetized dogs after giving the stimulants. Sodium nitrate and prostigmine were found to produce an enzyme rich secretion; epinine and SI (secretin plus pancreozymin) and enzyme poor one. All enzymes determined (amylase, lipase and trypsin) were equally affected by the various stimuli.

The Influence of a 5% Extract of Shottsuru (a Kind of Animal Seasoning) on the Intestinal Movements, the Secretion of Bile and the Pancreatic Secretion

Y. Hirawa. Mitt. Med. Akad. Kyoto 29, 635 (1940)  
CA. 35: 3712<sup>6</sup>

Shottsuru accelerated the pancreatic secretion but had no effect on the bile secretion.

The Action of P- Hydroxyphenylethylamine. II. Effect on the secretion of Pancreatic juice.

M. Kageyama. Acta Scholae Med. Kyoto 1, 229 (1916)

CA. 11:3338<sup>5</sup>

Injection of tyramine inhibits the flow of pancreatic juice..

Hypnotics and Their Action on the Thalamic Centers. IV. The Action of MgSO<sub>4</sub> on the Pancreas.

J. LaBarre and O. Vesselovsky. Arch. Intern. Pharmacodynamie 67, 267 (1942). CA. 38:4329<sup>7</sup>

The intravenous injection of MgSO<sub>4</sub> causes a diminution of the response of the pancreas in dogs, and the lipase content of the collected juice is low.

Action of Quaternary Amines on Pancreatic Secretion

L. Launoy. Compt. Rend. Soc. Biol. 73, 374 (1912)

CA. 7:517<sup>5</sup>

Ethyltrimethylammonium chloride, bromoethyltrimethylammonium bromide, and choline - HCl stimulate pancreatic secretion. The first two are toxic and methods of reducing the toxicity are discussed.

The Action Quaternary Amines on Pancreatic Secretion III.

Ibid 456 CA. 7:842<sup>1</sup>

Further work with other quaternary amines is discussed.

Action of some Amines, Especially Tetramethylammonium Chloride and Hydroxide, on Pancreatic Secretion  
Ibid 72, 1068 (1912). CA. 7:2971<sup>4</sup>

The effect of various amines are discussed. The activity of tetramethylammonium hydroxide or chloride is practically identical with that of choline.

The Influence of Eserine on the External Secretion of the Pancreas

L. Liaci. Biochem. Terap. Sper. 25, 445 (1938). CA. 33:2219<sup>3</sup>

In dogs small doses of eserine stimulated and larger doses inhibited pancreatic secretion.

Biliary, Pancreatic and Duodenal Studies. I. The H-ion concentration of Successive Portions of Duodenal Contents Following Stimulation with MgSO<sub>4</sub>

L. Martin. Arch. Internal Med. 39, 275 (1927). CA. 21:1669<sup>4</sup>

Installation of MgSO<sub>4</sub> by duodenal tube is followed by a slightly acid reaction of the secretion, the acidity increasing the longer the tube is retained. Active pancreatic enzymes are found in the alkaline fraction before the change of reaction.

The External Secretory Function of the Human Pancreas

J. M. McCaughan, B. L. Sinner and C. J. Sullivan. Arch.  
Int. Med. 61, 739 (1938)

Physiologic observations on the external secretory function of the human pancreas were made on a patient in whom a pancreatic fistula developed after a gastric resection. A rise in the secretory rate of juice followed the administration of secretin, a mixed meal, water, hydrochloric acid, beef broth, dextrose, olive oil, peptone, coffee, mecholyl and physostigmine. A fall occurred after the administration of sodium bicarbonate, bile salts, magnesium sulfate, stropine, epinephrine and histamine. The total base was elevated after the administration of secretin, sodium bicarbonate and coffee, and was depressed after administration of a mixed meal, beef broth, dextrose, bile salts, physostigmine, epinephrine and histamine. There was no significant change after administration of hydrochloric acid, peptone and magnesium sulfate.

Effect of Geneserine on Salivary and Pancreatic Secretion

M. Polonovski and P. Combemale. Compt. Rend. Soc. Biol. 88,  
881 (1923). CA. 17:2326<sup>8</sup>

The alkaloid geneserine increases the salivary and pancreatic secretions.



The Effects of the Subcutaneous Injection of Organ Extracts  
upon the Flow of Pancreatic Secretion

J. Rogers, J. M. Rahe, G. G. Fawcett and G. S. Hackett.

Am. J. Physiol. 40, 12 (1916)

The effect of the subcutaneous injection in dogs of the residue, or non-coagulable portion, of an aqueous extract of the liver is the immediate and vigorous stimulation of the external secretion of the pancreas. The residues of the thyroid and thymus produce a somewhat less vigorous and later response. The residues of the pituitary, parathyroid, spleen and pancreas are inert. The residue of the adrenal gland is inhibitory. Only the residues or non-coagulable portion show any appreciable effect.

The Action of Thyroxine on the Amylase, Lipase, and Trypsin  
of the Pancreas

G. Scoz. Boll. Soc. Ital. Biol. Sper. 9, 971-3 (1934)

CA. 29:1842<sup>6</sup>

In dogs treated with thyroxine, the amylase of the pancreas decreased about 80%; the lipase, an average of 40-50%; the trypsin, an average of 30%. There was no relation between variations in weight and variations in the enzymic activity of the treated dogs.

The Action of Karlsbad, Glauber and Epsom Salt on the  
External Secretion of the Liver and Pancreas

H. Simon. Deut. Med. Wochschr. 50, 1012 (1924). CA. 18:3085<sup>4</sup>

The intraduodenal administration of these salts  
increases the secretion of liver and pancreas.

Effects of Sodium Evipan on Certain Functions of the  
Digestive Tract. Salivary and Pancreatic Secretion and  
Intestinal Movements.

A. Tournade and E. Joltrain. Compt. Rend. Soc. Biol. 121,  
908 (1936). CA, 30:4216<sup>5</sup>

Evipan anaesthesia does not affect the flow of pan-  
creatic juice after the injection of secretin.

## SECTION V

### FUNCTION TESTS

- a. Analysis of Duodenal Contents
- b. Analysis of Blood Enzymes
- c. Other Function Tests

a. Analysis of Duodenal Contents



The Secretin Test of Pancreatic Function in the Diagnosis  
of Pancreatic Disease

G. Agren, H. Lagerlof and H. Berglund, Acta Med. Scand. 90,  
224 (1936)

Normal values for pancreatic enzyme output are given. There is very little functional disturbance in acute pancreatitis, but in disturbances associated with a decrease in diastase and trypsin. The gastric juice is not affected by the secretin injection during the test.

Pancreatic Enzymes in the Duodenal Juice in the Celiac  
Syndrome

D. H. Andersen. Am. J. Dis. Child. 63, 643 (1942)

The assay of trypsin in the duodenal juice is a reliable means of diagnosis of pancreatic deficiency. The assay of amylase is not a reliable means of diagnosis, because of its low concentration during the first months of life in normal infants and in older infants and children with chronic diarrhea. Amylase may occasionally be present with pancreatic fibrosis because of the failure of salivary amylase to be destroyed in the stomach. Lipase is present in normal infants of all ages. The values of enzyme concentration in normal and diseased infants is given.

Diagnostic Value of Pancreatic Function Tests in 47 Surgically Treated Cases

L. Bauman, A. O. Whipple. Am. J. Med. Sci. 207, 281 (1944)

The pancreatic enzyme content of patients with various pathological conditions are listed and the findings discussed.

The Measurement of the External Pancreatic Secretion in the Clinic by the Secretin Test

M. Chiray and M. Bolgert. Nutrition (Paris) 6, 223 (1936)

The results of use of the test in the clinic on patients with various pathological conditions are described.

The Diagnosis of Pancreatic Affections by a Test with Purified Secretin

M. Chiray and M. Bolgert. Presse Med. 44, 428 (1936)

CA. 31:1837<sup>2</sup>

A technic is described of collecting pancreatic juice after application of secretin, and evaluating the enzyme value of the sample.

Tests of Pancreatic Function

M. W. Comfort. J. A. M. A. 115, 2044 (1940)

The use of purified secretin plus mecholyl chloride as a diagnostic aid is described; both normal and abnormal

values for the secreted juice (obtained by a double-barreled gastroduodenal tube) are given. The use of stool analysis for undigested and unabsorbed food, blood enzyme determinations and urine amylase determination as tests for pancreatic dysfunction are discussed.

The Concentration of Pancreatic Enzymes in the Duodenum of Normal Persons and Persons with Disease of the Upper Part of the Abdomen

M. W. Comfort, R. L. Parker and A. E. Osterberg. Am. J. Dig. Dis. 6, 249 (1939)

Normal values for trypsin, lipase and amylase are given. A marked contraction of the range of concentrations of these was found in patients with carcinoma of head of pancreas, and of the ampulla of Vater, and chronic atrophic pancreatitis with steatorrhea.

Studies in Pancreatic Disease. I. Duodenal Content Analyses as an Index of Disease and Functional Activity of the Pancreas.

B. B. Crohn. Arch. Int. Med. 15, 581 (1915)

Correlates the quantitative results of enzyme analysis of duodenal contents with diseases of the pancreas.

The Clinical Application of Secretin in the Study of  
Pancreatic Function

J. S. Diamond and S. A. Siegel. N. Y. State J. Med. 41,  
869 (1941)

The use of the secretin test on 90 patients, both normal and with pathological conditions is described, and the findings discussed. It was found that in pathologic states of the pancreas the enzyme production first became affected; the volume and bicarbonate were more stable and less easily disturbed.

The Secretin Test in the Diagnosis of Pancreatic Diseases  
with a Report of One Hundred Thirty Tests

J. S. Diamond and S. A. Siegel. Am. J. Dig. Dis. 7, 435  
(1940)

The use of the secretin test and the results obtained with it on patients with various pathological conditions are discussed. When secretin alone is injected, pancreatic juice of low enzyme content is elaborated. When insulin or other vagal stimuli are used in conjunction with secretin the enzyme concentration is increased 2 or 3 fold.

The Use of Secretin as a Clinical Test of Pancreatic Function

J. S. Diamond, S. A. Siegel, M. B. Gall and S. Karlen. Am.  
J. Dig. Dis. 6, 366 (1939)

The results of studies of pancreatic function in normal and abnormal cases by means of the secretin test are given.



The Secretin Test as an Aid in the Differential Diagnosis  
of the Steatorrheas with a Report of Fourteen Cases

J. S. Diamond, S. A. Siegel and S. Myerson. Rev. Gastro-  
enterology 7, 429 (1940)

The use of the secretin test in diagnosing cases of  
pancreatic dysfunction is described. The results of its  
use on fourteen patients are given in detail.

The Involvement of the Pancreas in Liver Diseases with a  
New Method of Testing Pancreatic Function

P. Eckey. Ztschr. f. d. ges. Exp. Med. 94, 726 (1934)  
Nutr. Abs. and Rev. 4, 791 (1935)

A method of estimating pancreatic efficiency is de-  
scribed which consists in estimating the volume and tryptic  
activity of duodenal juice before and after the intra-  
duodenal administration of 3 ml. ether. Disturbances in  
secretion were noted in cases of hepatic cirrhosis, cholec-  
ystitis, jaundice and pernicious anemia.

Pancreatic Function and Disease in Early Life. I. Pancrea-  
tic Enzyme Activity and the Celiac Syndrome.

S. Farber, H. Schwachman and C. L. Maddock. J. Clin. Invest.  
22, 827 (1943)

Over 150 determinations of the activity of trypsin,  
amylase, and lipase were made. Patients with 'pancreatic  
fibrosis' exhibit a reduced enzyme content of duodenal juices.

Study of the Enzyme Activities of Duodenal Contents as a Means of Evaluating Pancreatic Function

A. H. Free, A. J. Beams and V. C. Myers. Gastroenterology 1, 188 (1943)

Quantitative determinations of enzyme activity were carried out in a group of normal subjects during fasting and after stimulation of the pancreatic secretion with olive oil. On the basis of results obtained in these subjects a system of evaluating pancreatic secretory activity is described.

Pancreatic Function and Disease in Early Life. II. Effect of Secretin on Pancreatic Function of Infants and Children.

C. L. Maddock, S. Farber and H. Schwachman. Am. J. Dis. Child. 66, 370 (1943)

By means of intravenous injection of 'pancrotest' secretin pancreatic function tests were carried out on children (6 wks. to 11 yrs.) with various nutritional and pancreatic disorders. In normals and in all cases except those of pancreatic fibrosis there was a postinjection increase in volume and pH. Patients with pancreatic fibrosis and trypsin deficiency both failed to show postinjection increase in tryptic activity. All cases except fibrosis showed increase of lipase after secretin, and there was increased amylase in all except fibrosis and celiac disease, in which there was a decrease.

New Methods for Estimating Enzymatic Activities of Duodenal Contents of Normal Man

C. W. McClure, A. S. Wetmore and L. Reynolds. Arch. Int. Med. 27, 706 (1921)

Methods of determining proteolytic, lipolytic and amylolytic enzymes are discussed, and their shortcomings in using them for analysis of the enzymes of duodenal contents are pointed out. The authors' methods for the determining of these enzymes in duodenal contents are given in detail, and their accuracy is discussed.

An Analysis of the Duodenal Drainage in the Steathorrhoeas

H. F. Philipsborn, Jr. et.al. J. Pediatrics 26, 107 (1945)

The duodenal contents of normal children, 'feeding problems', and children with pancreatic disease were analyzed for enzymatic activity, and the values obtained are given. 'Feeding problems' may be due to temporary pancreatic insufficiency.

The External Secretion of the Pancreas and Diabetes Mellitus

H. M. Pollard, L. Miller and W. A. Brewer. Am. J. Dig. Dis. 10, 20 (1943)

In a clinical study using the secretin test there were diminutions in volume of secretion, total secretion of bicarbonate, and the enzymes amylase and trypsin. These findings are correlated only with the duration of the disease and not with the age of the patient, the severity of the disease, the presence or absence of acidosis, the amount of insulin required or the diet.

b. Analysis of Blood Enzymes



Acute Pancreatitis, with Special Reference to Pathogenesis  
and the Diagnostic Value of the Blood Amylase Test

W. R. Cole. Am. J. Surgery 40, 245 (1938)

In acute pancreatitis the level of the blood amylase is high usually only during the first 2 or 3 days of the attack. The amount of serum amylase found in clinical cases is given,

Serum Lipase: Its Diagnostic Value

M. W. Comfort. Am. J. Dig. Dis. 3, 817 (1937)

A method of determining serum lipase is described. Values obtained with normal subjects and with patients with various diseases are given.

Serum Lipase: Its Diagnostic Value

M. W. Comfort. Proc. Staff Mayo Clinic 10, 810 (1935)

Discusses the values obtained in the clinic with various pathological conditions. An increased activity of the serum lipase appears to be a very efficient test for pancreatitis, less so for malignant disease of the pancreas.

Serum Amylase and Serum Lipase in the Diagnosis of Disease of the Pancreas

M. W. Comfort and A. E. Osterberg. Med. Clin. N. A 24, 1137 (1940)

Discusses the determination of serum amylase and lipase and the use of them in diagnosing diseases of the pancreas. The authors are of the opinion that as of the time of writing the article the determination of the value for serum lipase is the more reliable as a test for pancreatic function.

Lipase and Esterase in the Blood Serum. Their Diagnostic Value in Pancreatic Disease.

M. W. Comfort and A. E. Osterberg. J. Lab. Clin. Med. 20, 271-8 (1934). CA. 29:2594<sup>7</sup>

An increased activity of serum lipase was observed in acute and subacute pancreatitis and in cases of obstruction to the outflow of pancreatic juice due to carcinoms of the head of the pancreas. An increase observed in duodenitis, cancer of the stomach and other conditions was apparently due to associated pancreatic disease. The concentration of esterase, which is normally present in blood serum, appears to bear no relation to the condition of the pancreas.

Lipase and Esterase in the Blood Serum: Their Diagnostic Value in Pancreatic Disease

M. W. Comfort and A. E. Osterberg. Proc. Staff May Clinic 9, 250 (1934)

A discussion of the methods of determining serum lipase and esterase, and the use of them in diagnosis of pancreatic dysfunction.

The Variations of Blood Amylase During Acute Transient Disease of the Pancreas

R. Elman. Ann. Surg. 105, 379 (1937)

The results of the use of the serum amylase test with patients suffering from transient attacks of acute abdominal pain and having other symptoms of gastrointestinal disturbance are discussed. There was a very high concentration of blood amylase at the height of the attack, but returned to normal with a subsidence of the symptoms.

Value of Blood Amylase Estimations in the Diagnosis of Pancreatic Disease

R. Elman, N. Arneson and E. A. Graham. Arch. Surg. 19, 943 (1929)

A clinical study in which the blood amylase was determined in 60 patients. Deviations from the normal range were found in patients with pancreatic disorders.

Diagnostic Significance of Determinations of Serum Lipase

T. A. Johnson and H. L. Bockus. Arch. Int. Med. 66, 62  
(1940)

A report of the study of 371 cases in which the serum lipase was determined. The reports of others showing that diseases of the pancreas show the highest incidence of increased values for serum lipase are confirmed.

A Clinical Evaluation of the Laboratory Analysis of the Function of the Pancreas.

B. B. Kogen. Klin. Med. (USSR) 17, 67 (1939). CA. 33;6431<sup>9</sup>

The most satisfactory diagnostic index of chronic pancreatitis is the increase in diastase in the blood and urine. No cases were observed of an increase in diastase under normal functioning conditions.

The Clinical Value of the Serum Amylase Test

E. F. Lewison. Surg., Gyn. and Obs. 72, 202 (1941)

The serum amylase of 720 patients with various diseases were determined and the values obtained are given. The methods of serum amylase determinations are reviewed. Age, sex, diet, vitamin deficiency and starvation have no effect on serum amylase values. Deviations from normal were found in mumps, liver disease and acute pancreatitis.



The Dynamics of Blood-Diastase Activity in Different Types of Patients

B. V. Lyntrovkin. Khirurgiya No. 2-3, 62 (1940). CA. 38:2728<sup>2</sup>

The blood diastase was determined in 110 subjects in the fasting condition and after a meat test-meal. In patients with diseases of the pancreas the diastatic activity is lower than the normal in fasting conditions and higher after the ingestion of the test meal. Concludes that the test may serve as a diagnostic aid in diseases of the pancreas.

An Evaluation of the Clinical Significance of Serum Amylase and Lipase Determinations

M. M. McCall and J. G. Reinhold. Surg. Gyn. Obs. 80, 435 (1935)

The relative diagnostic value of serum amylase and serum lipase in patients with diseases of the pancreas, liver and gall bladder is compared and the methods of determining them are discussed. Values obtained with normal and diseased subjects are given.

Diagnosis of Pancreatic Disease; Limitations of Present Blood Diastase Test, Suggestion for Increasing Its Effectiveness

J. M. McCaughan. Proc. Soc. Exp. Bio. Med. 40, 665 (1939)

Experiments are described using a balloon in the duodenum of a dog to block the pancreatic secretions. Using

this technique in a test for pancreatic function, a normal patient might be expected to show a rise in blood diastase, whereas one with the function impaired might remain unaltered or change but slightly.

The Value of Estimations of the Amylase of the Blood in the  
Diagnosis of Suspected Pancreatic Disease

J. M. McCaugham.. Surg., Gyn. and Obs. 59, 598 (1934)

A review of the literature and a discussion of the use of the test.

The Clinical Significance of the Serum Amylase Test in the  
Diagnosis of Acute Pancreatitis

H. McCorkle and L. Goldman. Surg., Gyn. and Obs. 74, 439  
(1942 )

Gives 10 case histories in which the test was used for diagnosis and discusses the use of the test.

Study of the Diastase in Blood and Urine under Definite  
Dietary Conditions

A. Mekler. Gastroenterologia 66, 12 (1941)

24 patients under definite diet were examined daily for the diastase secretion in the urine and the diastase content in the blood serum. Those having no manifest ailments of the abdominal organs had normal diastase in urine and blood. Those having higher diastase levels in urine and blood, who didn't exhibit pancreatic disease, were affected in other abdominal organs. The latter is explained

by inferring that in spite of lack of clinical symptoms of pancreatic disease, pancreatic function may be affected by diseases of neighboring organs--the latter producing a slight disease of the pancreas. The method may be developed as a clinical test for pancreatic function.

The Relationship of Pancreatic Enzymes to Food Allergy

A. W. Oelgoetz, P. A. Oelgoetz and J. H. Wittekind. Am. J. Dig. Dis. 1, 730 (1934), Ibid. 2, 422 (1935), Ibid. 3, 199 (1936), Med. Rec. 143, 20 (1936), Ibid. 150, 276 (1939).

The following hypothesis is set forth in all the papers: The amount of enzymes secreted by the normal functioning pancreas is in excess of that required for digestion in the intestine. The 'surplus' of enzymes is absorbed and enters the blood. Food is absorbed in various degrees of digestion--from protein to amino-acid--and digestion is continued in the blood by virtue of the circulating enzymes. In instances of pancreatic insufficiency the enzyme output may be just enough to take care of intestinal requirements and none, or a very slight amount, enters the blood. Therefore the proteins, metaproteins, etc., in the blood are not digested and the animal becomes sensitive to foods. Further ingestion of food while in this condition causes an allergic reaction to occur. To counteract this the administration of less food, or of dry pancreatic enzymes is suggested.



A test is described to quickly and easily measure blood enzyme levels. A starch-iodine mixture is used and the serum is allowed to act on it. This measures the amylase, but the blood enzymes follow a parallel concentration and therefore it is considered an index of the total blood enzyme content.

#### Blood Amylase

D. Polowe. Am. J. Clin. Path. 13, 288 (1943)

The methods of determination and the conditions in which there are a deviation from the 'normal' are discussed.

#### A New Test for Pancreatic Function. II. Experimental Observations.

H. J. Popper, W. H. Olson and H. Necholes. Surg., Gyn. and Obs. 77, 471 (1943)

A test is described giving mechoyl plus secretin to the subject and then determining the serum lipase. In the normal the latter shows an increase. The work to date has been done with dogs.

#### A New Test for Pancreatic Function: Experimental Observations

H. L. Popper and H. Necholes. Gastroenterology 1, 490 (1943)

The subcutaneous injection of a combination of acetyl-beta-methylcholine hydrochloride plus eserine sulfate results



in an increase of serum amylase and lipase only in the presence of normal pancreas, but not in the presence of an atrophic pancreas.

Amylase in the Blood in Subacute and in Chronic Pancreatic Diseases

E. G. Wakefield, J. M. McCaughan and C. S. McVicar. Arch. Int. Med. 45, 473 (1930)

The percentage of positive data is too small to warrant the adoption of a routine diagnostic procedure of study of the amylase of the blood in cases of suspected pancreatic disease.

c. Other Function Tests

## Tests of Pancreatic Function

M. W. Comfort. J. A. M. A. 115, 2044 (1940)

The use of purified secretin plus mecholyl chloride as a diagnostic aid is described; both normal and abnormal values for the secreted juice (obtained by a double-barreled gastroduodenal tube) are given. The use of stool analysis for undigested and unabsorbed food, blood enzyme determinations and urine amylase determination as tests for pancreatic dysfunction are discussed.

## IV. Contributions to the Physiology of the Pancreas. The Elimination of Dyes in the External Secretion of the Pancreas

L. A. Crandall, E. Oldberg and A. C. Ivy. Am. J. Physiol. 89, 223 (1929)

Of 90 dyes tested, none were eliminated in sufficient quantity to be of practical value as a pancreatic function test.

## The Activity of the Pancreatic Function under the Influence of Copious Water Drinking with Meals

P. B. Hawk. Am. J. Physiol. 27, XXVI (1910)

The activity of the pancreatic function as measured by the focal amylase was found to be greatly facilitated when additional volumes of H<sub>2</sub>O ranging from 1500-4000 cc. were daily ingested at meals by normal men on a uniform diet.

The Dependence of the External Secretion of the Pancreas  
And Liver on the Amount of Work Required of These Organs  
I. D. Klimenko, Acta. Med. Scand. 83, 565 (1934), Nutr.  
Abs. and Rev. 4, 791 (1935)

Both in lower animals and man the presence of oil or fat in the duodenum leads to closure of the pylorus. This action is chemical, not mechanical; vaseline is without effect. The greater the quantity of oil or fat, the more prolonged is the closure of the pylorus. Since the disappearance of the fat or oil depends on the secretion of the pancreas and liver, the length of time of pyloric closure is an index of pancreatic and liver efficiency.

A Study of the Diastatic Activity of the Urine and Feces  
with Special Reference to Diseases of the Pancreas

C. W. McClure and J. H. Pratt. Arch. Int. Med. 19, 568 (1917)

They conclude that the measurement of the diastatic activity of the urine and feces is of little value in diagnosing pancreatic diseases.

A Practical Test of Pancreas Function with Iodized Oil

T. Tremolieres. Rev. Med. 57, 1 (1940). CA. 34:6313<sup>4</sup>

A test is described in which the patient take capsules of iodized oil on an empty stomach and the iodine content of the urine is observed for the next 24 hours.



The digestion and absorption of oil are impaired in pancreatic disturbances and consequently only small amounts of iodine appear in the urine.

#### Pancreatic Function Tests

J. A. Wolfer and L. M. Christian. Arch. Surg. 17, 899 (1928)

The literature on pancreatic function tests is reviewed. An attempt to use the determination of fecal amylase as a test for pancreatic function was made. Fecal amylase values of normal persons vary from day to day, depending on the diet. As a test of function it is only useful when there is complete lack of pancreatic secretion. With dogs it was shown that increases in pancreatic secretion upon the application of stimulants can be measured by the fecal amylase.

SECTION VI  
BOOKS AND REVIEWS

Secretory Mechanism of the Digestive Glands

B. P. Babkin. New York. Paul Hoeber, Inc. (1944)

Contains the results of, and discusses the experimental work done on pancreatic secretion, both 'normal' and as a result of various stimuli.

Blood Sugar Concentration and the External Secretion of the Pancreatic Gland

B. I. Babkin. J. A. M. A. 105, 1659 (1935)

A review of the work done. Hyperglycemia always increases the output of enzymes from the acinous cells and in certain cases increases the volume of the secretion. Hypoglycemia produced by the administration of insulin lowers the concentration of enzymes in the pancreatic juice. After section of the vagus this effect disappears. The conflicting results obtained with humans are ascribed to the methods of recovering the juice.

The External Secretion of the Digestive Glands (Die Aussere Sekretion Der Verdauungsdrusen)

B. P. Babkin. Berlin. Julius Springer (1928)

Pages 462-543 contain a very extensive review of the work done on the determination of normal pancreatic secretion and of the effect of various stimuli upon it. Quantitative results of much of the experimental work cited are included.

### Tests of Pancreatic Function

M. W. Comfort. J. A. M. A. 115, 2044 (1940)

The use of purified secretin plus mecholyl chloride as a diagnostic aid is described; both normal and abnormal values for the secreted juice (obtained by a double-barreled gastroduodenal tube) are given. The use of stool analysis for undigested and unabsorbed food, blood enzyme determinations and urine amylase determination as tests for pancreatic dysfunction are discussed.

### The Origin and Significance of Blood Serum Enzymes

L. A. Crandall. Am. J. Dig. Dis. 2, 230 (1935)

A review containing a section on the relation of blood enzymes to pancreatic function.

### The Pancreas: Contributions of Clinical Interest Made In 1943

R. Elman and J. T. Akin, Jr. Gastroenterology 2, 412 (1944)

### The Pancreas: Contributions of Clinical Interest Made In 1942

R. Elman and C. E. Lischer. Gastroenterology 1, 635 (1943)

### Contributions in Regard to the Pancreas in 1941

R. Elman and A. M. Large. Am. J. Dig. Dis. 2, 303 (1942)



1940 Contributions in Regard to the Pancreas

R. Elman and L. A. Sachar. Am. J. Dig. Dis. 8, 108 (1941)

Contributions Made in 1939 to Knowledge in Regard to the Pancreas.

R. Elman. Am. J. Dig. Dis. 7, 227 (1940)

Contributions Made in 1938 to Knowledge in Regard to the Pancreas

R. Elman. Am. J. Dig. Dis. 6, 233 (1939)

A series of reviews covering the effects of food and other stimuli on pancreatic secretion, pancreatic insufficiency, function tests, and the clinical, surgical and pathological aspects of pancreatic disorders.

Certain Aspects of the Applied Physiology of the External Pancreatic Secretion

A. C. Ivy. Am. J. Dig. Dis. 3, 677 (1937)

A review article dealing with the effects of exclusion of pancreatic juice from the intestine, blood enzymes and exclusion of pancreatic juice, functional tests of external secretory activity of the pancreas, and the effect of foods on the pancreatic secretion.

The Role of Hormones in Digestion

A. C. Ivy. Physiol. Rev. 10, 282 (1930)

A review article containing a section dealing with the effects of various stimuli on pancreatic secretion.

Pancreatic Function and Pancreatic Disease

H. O. Lagerlof. New York. The Macmillan Co., (1942)

A comprehensive work containing a history of the experimental work done on pancreatic secretion, the methods used in recovering pancreatic juice and in analyzing it for its enzyme content, the use of secretin preparations in functional tests, the responses of the pancreas to various stimuli, and case histories of patients with various pancreatic diseases. The quantitative results of much of the experimental work are included.

The Value of Estimations of the Amylase of the Blood in the Diagnosis of Suspected Pancreatic Disease

J. M. McCaugham. Surg., Gyn. and Obs. 59, 598 (1934)

A review of the literature and a discussion of the use of the test.

Blood Amylase in Diseases of the Pancreas

V. C. Myers. Gastroenterology 1, 617 (1943)

A review.



Functional Activities of the Pancreas and Liver

C. W. McClure. Medical Authors Pub. Co. (1937)

A monograph dealing with tests of pancreatic function, and the response of the pancreas to food and various stimuli.

Observations on the Physiology and Pathologic Physiology of External Pancreatic Functions

C. W. McClure. Rev. Gastroenterology 3, 1 (1936)

A review dealing with the effects of food and various stimuli on pancreatic function and the physiology of pancreatic secretion.

Disturbances of the External Secretion of the Pancreas

K. Nissen. Deutsch. Med. Wochenschr. 59, 1464 (1933), Nutr. Abs. and Rev. 3, 731 (1934)

A review of literature on disturbance of pancreatic function.

The Work of the Digestive Glands

I. P. Pavlov. London. Charles Griffin and Co. 1910

A series of lectures with the physiology of the digestive glands. Experimental work on the relation of the output of pancreatic juice to the food intake is reviewed in detail.

The Pancreatic Secretion (La Secretion Pancreatique)

E. F. Terroine. Paris. Librairie Scientifique A. Hermann  
and Fils (1913)

A monograph containing a review of the literature on  
the experimental work done on pancreatic secretions to  
that date.